Cyanobacteria: Stopping Cancer in its Tracks

by Amy Keller

In the 2008, the Journal of the American Chemical Society published the article entitled, "Structure and activity of largazole, a potent antiproliferative agent from the Floridian marine cyanobacterium *Symploca* sp." by Ms. Kanchan Taori, Dr. Valerie Paul, and Dr. Hendrik Luesch. The *Newsletter* interviewed author and ASP member Dr. Hendrik Luesch, who shared his discoveries of the *Symploca*.

GINA PATEL

From left to right: Drs. Qi-Yin Chen, Susan Matthew, Yanxia Liu, and Hendrik Luesch, Ms. Lilibeth Salvador, Mr. Jason Kwan, Ms. Rana Montaser, and Ms. Rui Wang.

How did you become interested in natural products of marine origin?

As a chemistry student in Germany I became intrigued by the complex structures of marine natural products and that oceans were largely unexplored for drug discovery. I chose the University of Hawai'i for my Ph.D. research under ASP member Dr. Richard Moore on the chemistry of marine cyanobacteria. I have been hooked ever since.

Who in your laboratory carried out the research?

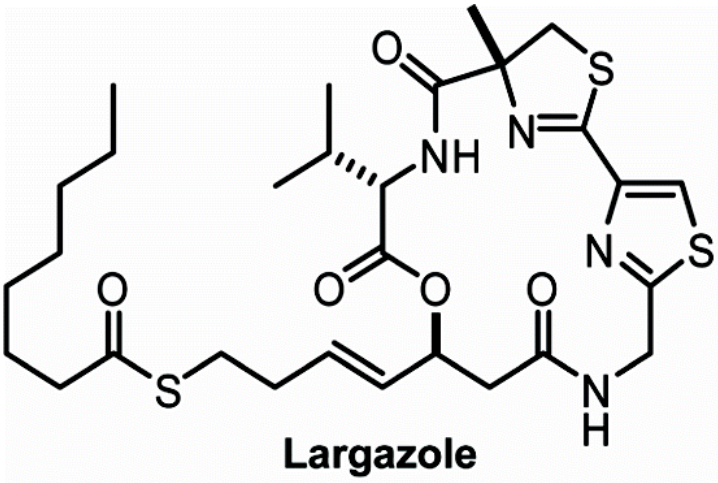
Ms. Kanchan Taori, my graduate student at the time (she recently graduated with a M.S. degree) isolated largazole (*J. Am. Chem. Soc.* **2008**, 130, 1806) and carried out initial mechanistic studies described in a follow up paper on the synthesis and molecular target (*J. Am. Chem. Soc.* **2008**, 130, 8455). We teamed up with Dr. Jiyong Hong at Duke University, Durham, North Carolina, for the total synthesis to allow rigorous biological evaluation and to start establishing the SAR (Org. Lett. 2008, 10, 4021). My postdoc Dr. Yanxia Liu is currently advancing the biological studies.

Could you provide a brief explanation of the work and results in your own words? In what way are the data in your paper new?

Largazole has an unprecedented structure and potent antiproliferative activity against a variety of cancer cell types. It is also one of only relatively few marine secondary metabolites with a thioester moiety. We later described that this labile unit serves as a protecting group and upon hydrolysis liberates the corresponding thiol, one of the most potent known histone deacetylase (HDAC) inhibitors of class I isoforms.

What impact does this have on natural product and cancer research?

The discovery of largazole is another encouraging example of the value of marine natural products, in particular marine cyanobacteria, for drug discovery. HDACs are validated targets for anticancer therapy and already targeted by the Merck drug SAHA (approved for cutaneous T-cell lymphoma) that does not discriminate well among HDAC isoforms. The largazole structure may provide a template for the rational design of HDAC isoform selective inhibitors and drugs. As a result of our publications, several groups around the world have now already also engaged in this area of research.



Largazole

What is a favorite nonscientific activity of your lab?

Group parties at my house.

What is your greatest extravagance in the lab?

New technology.